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Patentanwälte

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ART 34 AMDT

English translation of the amended claims

1. Use of a Hsp70 protein which does not form a complex with peptides when isolated together with these from tumour cells, a C-terminal fragment thereof or a derivative thereof or a protein with an amino acid sequence homology to the region of amino acids 384-641 of the Hsp70 protein of ≥ 70 % for the production of a pharmaceutical preparation, a medical product or a medical adjuvant for the activation of NK-cells.
2. Use of a Hsp70 protein which does not form a complex with peptides when isolated together with these from tumour cells, a C-terminal fragment thereof or a derivative thereof or a protein with an amino acid sequence homology to the region of amino acids 384-641 of the Hsp70 protein of ≥ 70 % for the in vitro or ex vivo activation of NK-cells.
3. Use according to claim 1 or 2, wherein the activation comprises the induction of an immune response mediated by NK-cells.
4. Use according to any one of claims 1 to 3, wherein the activation includes a stimulation of the proliferation of NK-cells and/or an increase of the cytolytic activity of NK-cells.
5. Use according to claim 4, wherein the cytolytic activity against tumour cells, cells from patients with infectious diseases is increased.
6. Use according to claim 5, wherein the cytolytic activity against leukaemia cells, lymphoma cells, tumour cells, metastasizing cells of solid tumours and cells of patients with viral, mycotic and/or bacterial infectious diseases is increased.
7. A method for the ex vivo or in vitro activation of NK-cells, wherein a physiological cell suspension containing NK-cells is mixed and incubated with a Hsp70 protein which does not form a complex with peptides when isolated together with these from tumour cells, a C-terminal fragment thereof or a derivative thereof or a protein

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with an amino acid sequence homology to the region of amino acids 384-641 of the Hsp70 protein of $\geq 70\%$ to effect activation of the NK-cells.

8. The method according to claim 7, wherein the activation comprises a stimulation of the proliferation of the NK-cells and/or an increase of their cytotoxicity.
9. The method according to claim 7 or 8, wherein peripheral, mononucleic blood cells or a fraction containing NK-cells is used as physiological cell suspension containing NK-cells.
10. The method according to any one of claims 7 to 9, wherein the cell suspension further contains human or animal cells expressing Hsp70 on the cell surface.
11. The method according to claim 10, wherein tumour cells, cells of patients with infectious diseases are used as human or animal cells.
12. The method according to claim 11, wherein leukaemia cells, lymphoma cells, tumour cells, metastasizing cells of solid tumours and cells of patients with viral, mycotic and/or bacterial infectious diseases are used as human or animal cells.
13. The method according to any one of claims 7 to 12, wherein the physiological cell suspension containing the cells and proteins is incubated for at least 3 hours.
14. The method according to claim 13, wherein the incubation is carried out for 4 days.
15. The method according to any one of claims 1 to 6 or the method according to any one of claims 7 to 14, wherein a cytokine is used in addition.
16. Use or method according to claim 15, wherein an interleukin is used as cytokine.
17. Use or method according to claim 16, wherein IL-2, IL-12 and/or IL-15 is used as interleukin.
18. A method for the *in vivo* activation of the immune system, wherein a patient is given a pharmaceutically effective amount of NK-cells activated according to the method according to any one of claims 7 to 17, optionally in combination with or before a pharmaceutically effective amount of Hsp70 protein, a C-terminal fragment thereof or a derivative thereof or a protein with an amino acid sequence homology to the region of amino acids 384-641 of the Hsp70 protein of $\geq 70\%$.

19. The method for the in vivo activation of NK-cells, wherein a patient is given a pharmaceutically effective amount of a Hsp70 protein which does not form a complex with peptides when isolated together with these from tumour cells, a C-terminal fragment thereof or a derivative thereof or a protein with an amino acid sequence homology to the region of amino acids 384-641 of the Hsp70 protein of $\geq 70\%$.
20. The method for the treatment of tumours, cancer diseases, infectious diseases or autoimmune diseases, wherein a patient is given a pharmaceutically effective amount of NK-cells activated according to the method according to any one of claims 7 to 17 and/or a Hsp70 protein which does not form a complex with peptides when isolated together with these from tumour cells, a C-terminal fragment thereof or a derivative thereof or a protein with an amino acid sequence homology to the region of amino acids 384-641 of the Hsp70 protein of $\geq 70\%$.
21. The method according to claim 20, wherein the tumour is a solid tumour or a metastasis.
22. The method according to claim 20, wherein the cancer disease is leukaemia or a lymphoma.
23. The method according to claim 20, wherein the infectious disease has a viral, mycological or bacterial origin.
24. Pharmaceutical preparation, medical product or medical adjuvant containing a Hsp70 protein, a C-terminal fragment thereof or a derivative thereof or a protein with an amino acid sequence homology to the region of amino acids 384-641 of the Hsp70 protein of $\geq 70\%$ and/or NK-cells activated according to the method according to any one of claims 7 to 17 in a therapeutically effective amount as well as optionally common carrier substances and/or adjuvants except for Hsp70 protein which forms a complex with peptides when isolated together with these from tumour cells.
25. Pharmaceutical preparation, medical product or medical adjuvant according to claim 24, wherein the protein is present in a concentration of at least 1 $\mu\text{g}/\text{ml}$, preferably up to 1000 $\mu\text{g}/\text{ml}$.

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26. Use according to any one of claims 1 to 6 or the method according to any one of claims 7 to 23 or pharmaceutical preparation, medical product or medical adjuvant according to claim 24 or 25, wherein the Hsp70 protein is a human protein.
 27. Use according to any one of claims 1 to 6 or 26 or the method according to any one of claims 7 to 23 or 26 or pharmaceutical preparation, medical product or medical adjuvant according to any one of claims 24 to 26, wherein the Hsp70 protein or its fragment or derivative is a recombinant protein.
 28. Use according to any one of claims 1 to 6, 26 or 27 or the method according to any one of claims 7 to 23, 26 or 27 or pharmaceutical preparation, medical product or medical adjuvant according to claim 24 to 27, wherein the Hsp70 protein comprises the C-terminal fragment (amino acids 384 to 561) of the human Hsp70 or the corresponding region of another Hsp70 comprising the effects of the invention.
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29. Use of the NK-cells treated according to a method according to one or more of the above claims for the therapy of tumour diseases and/or infectious diseases.
 30. Use according to claim 29, wherein the therapy is carried out by re-infusion of the treated NK-cells.

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